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What is claimed is:

1. A method of designing inhibitors of TFPP-like aspartyl protease enzymes comprising:

(a) synthesizing a compound which targets aspartic acid residues of an enzymatic active site of a TFPP-like aspartyl protease enzyme or mimics a region surrounding a cleavage site of a TFPP-like aspartyl protease substrate; and

(b) determining the ability of the synthesized compound to inhibit cleavage activity of the TFPP-like aspartyl protease enzyme.

2. The method of claim 1 wherein the TFPP-like aspartyl protease enzyme is a type 4 prepilin peptidase.

3. The method of claim 2 wherein the ability of the synthesized compound to inhibit cleavage activity is determined via a method comprising:

(a) preparing a membrane fraction from a bacterial strain expressing a type 4 prepilin peptidase;

(b) contacting the membrane fraction with the synthesized compound; and

(c) determining cleavage activity of the type 4 prepilin peptidase in the presence of the synthesized compound, wherein a decrease of the cleavage activity of the type 4 prepilin peptidase in the presence of the synthesized compound as compared to the activity of type 4 prepilin peptidase in the absence of the synthesized compound is indicative of the test compound being an inhibitor of type 4 prepilin peptidase.

4. A method of identifying potential inhibitors of TFPP-like aspartyl protease enzymes comprising:

30 (a) selecting a test compound having a structure known to or suspected of targeting aspartic acid residues or

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mimicking a region surrounding a cleavage site of a TFPP-like aspartyl protease substrate; and

(b) determining the ability of the identified test compound to inhibit cleavage activity of the TFPP-like 5 aspartyl protease enzyme.

5. The method of claim 4 wherein the TFPP-like aspartyl protease enzyme is a type 4 prepilin peptidase.

6. A TFPP-like aspartyl protease enzyme inhibitor comprising a compound which targets the aspartic acid residues 10 of an aspartyl protease enzyme or mimics a region surrounding a cleavage site of an aspartyl protease substrate and inhibits cleavage activity of the TFPP-like aspartyl protease inhibitor.

7. An antibacterial agent comprising a TFPP-like 15 aspartyl protease enzyme inhibitor of claim 6.

8. The anti-bacterial agent of claim 7 wherein the compound modifies the aspartic acid residues of type 4 prepilin peptidase.

9. The anti-bacterial agent of claim 8 wherein the 20 compound comprises EDAC and glycine amide.

10. An anti-bacterial agent comprising a compound designed in accordance with claim 1.

11. An anti-bacterial agent comprising a compound identified in accordance with claim 4.

25 12. A composition comprising the anti-bacterial agent of claim 7 and a second known therapeutically active anti-bacterial agent.

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13. A method of inhibiting development of drug resistant strains of bacteria comprising administering in combination the anti-bacterial agent of claim 7 and a second known therapeutically effective anti-bacterial agent.

5 14. A method of inhibiting virulence factor production by bacteria comprising administering to bacteria an anti-bacterial agent of claim 7.

10 15. A method of inhibiting activity of a TFPP-like aspartyl protease enzyme in a host comprising administering to the host a TFPP-like aspartyl protease enzyme inhibitor of claim 6.

16. A method of inhibiting a bacterial infection in a host comprising administering to the host an anti-bacterial agent of claim 7.

15 17. A mutant construct of TcpJ wherein an amino acid at position 18, 46, 48, 51, 65, 73, 76, 81, 88, 125, 172, 183, 189, 191, 212, or 213 of SEQ ID NO:4 is mutated.

18. The mutant construct of claim 17 wherein the amino acid is mutated to alanine or leucine.

19. The mutant construct of claim 17 wherein the amino acid at position 125 or 189 of SEQ ID NO: 4 is mutated to asparagine or glutamic acid.

20. The mutant construct of claim 17 wherein the amino acid at position 183 of SEQ ID NO:4 is mutated to asparagine.

21. A nucleic acid sequence encoding a type 4 prepilin peptidase homologue in *Staphylococcus aureus* comprising SEQ ID NO:2.

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22. The nucleic acid sequence of claim 21 comprising
SEQ ID NO:1.